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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,275	11/13/2003	George H. Lowell	021989-000710US	5646

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,275	LOWELL ET AL	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 November 2003 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 13 pp.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-18 are pending in the instant application.

2. The disclosure is objected to because of the following informalities: the symbols in figure 4 cannot be distinguished. Appropriate correction is required.

3. This application contains sequence disclosures (see pages 15, 16 and 21) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this office action. A complete response to this office action should include both compliance with the sequence rules and a response to the NON-FINAL Office Action set forth below. Failure to fully comply with ***both*** these requirements in the time period set forth in this office action will be held non-responsive.

4. Claims 6 and 16-18 are objected to because of the following informalities: claim 6 recites "peptideantigen", which should be –peptide antigen--. Claims 16-18 recite "of treatment of prophylaxis", which should be --of treatment or prophylaxis--. Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5 and 7-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine composition comprising the peptide antigen SEQ ID NO: 2 and a proteosome adjuvant or a vaccine comprising MtsA and a proteosome, does not reasonably provide enablement for a vaccine comprising at least one (i.e. any) group A Streptococcus antigen and a proteosome adjuvant and methods of treatment or prophylaxis of all group A Streptococcal infection in an individual comprising administering a vaccine composition comprising at least one (i.e. any) group A Streptococcus antigen and a proteosome adjuvant to the individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is enabled for a J14/proteosome adjuvant composition. The J14 peptide is SEQ ID NO: 2. The examples set forth in the specification teach a J14/proteosome, nJ14/proteosome (J14 amino terminal anchor/proteosome adjuvant) and a cJ14/proteosome (J14 carboxyl terminal anchor/proteosome), as well as various defined ratios of construct components. J14 is a portion of the M protein of Streptococcus pyogenes. The specification is not enabled for the GAS vaccine wherein the antigen is protein H peptide.

The state of the art with regard to vaccines for group A Streptococcal infections is unpredictable. The state of the art indicates that Group A

Streptococci (GAS) are among the most common and widespread human pathogens; they cause acute pharyngitis, impetigo, acute rheumatic fever, rheumatic heart disease and acute glomerulonephritis (Hayman et al Immunology and Cell Biology, 2002, 80:178-87; see p. 178). Hayman et al also teaches that protection against GAS infection is believed to be mediated predominantly by opsonic antibodies directed against the surface M protein, the major virulence factor of GAS (p. 178, col. 1). Hayman et al teaches that the "elucidation of protective epitopes within the M protein of GAS has proceeded rapidly, thus permitting the development of the peptide vaccines that could elicit protection whilst avoiding autoimmunity. Unfortunately, the prospects of a useful vaccine have lagged, in part due to the lack of a suitable means of inducing high titre anti-M protein responses when immunizing with synthetic peptides." (p. 178, col. 2) Olive et al (Vaccine, 2002, 20:2816-2825) teaches that GAS infection includes pharyngitis, impetigo, scarlet fever, toxic shock syndrome, narcotizing fasciitis, rheumatic fever, rheumatic heart disease and throat infections (p. 2816, col. 1). "Current treatment for controlling GAS infection and GAS-associated diseases is with long-term high dose antibiotic therapy (citation omitted). However, this approach is largely inadequate due to poor compliance, highlighting the need for a GAS vaccine to prevent GAS-associated diseases." (p. 2816, col. 2) Although the M protein of GAS appears to be a viable strategy for a GAS vaccine, the "development of a broad-based vaccine against GAS infection has been impeded by the sequence variability that occurs between different GAS M proteins, and the possibility of inducing immune responses that are cross-reactive with cardiac and other host issues. A GAS vaccine candidate based purely on the M protein type-specific determinants is likely to provide protection only against specific GAS

strains, and since there are at least 100 different GAS serotypes this approach would no be efficacious." (p. 2817, col. 1; see also Brandt et al, Infection and Immunity, 2000, 68/12:6587-6594) Olive et al (Vaccine, 2005, 23:2298-2303) teaches that the "variability in M proteins and the potential for the induction of autoimmunity due to antigenic molecular mimicry between GAS M protein and self antigens (citation omitted) represents significant hurdles in the development of a broad-strain coverage vaccine. Multivalent M protein constructs containing epitopes from several type-specific regions of different M proteins (citations omitted) and those based on the conserved C-region (citation omitted) have shown promising results in animal trials. However, the efficacy of the GAS vaccine constructs required the use of adjuvants that can cause adverse side effects." (p. 2298)

The state of the art indicates that at the present time there is not a vaccine for GAS infections. Further, the art teaches that only the M protein of GAS has been deemed a possible antigen for a vaccine against GAS infection, not any GAS antigen as now claimed (see claim 1). Even though M protein appears to be a possible vaccine candidate, multiple M proteins from different GAS serotypes are needed in the vaccine to develop a broad-strain coverage vaccine, not one that simply contains one GAS antigen. The current state of the art indicates that the claimed invention is unpredictable with regard to the scope of the claimed invention. The specification does not provide any evidence for the scope of enablement of a vaccine to protect against any GAS infection using at least one of any GAS antigens and a proteosome adjuvant.

Finally, it should be noted that whether the specification would have been enabling as of the filing date involves consideration of the nature of the invention,

the state of the prior art, and the level of skill in the art. The initial inquiry is into the nature of the invention, i.e., the subject matter to which the claimed invention pertains. The nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art.

The state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains at the time the application was filed. See MPEP § 2164.05(b).

The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification.

The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date.

35 U.S.C. 112 requires the specification to be enabling only to a person "skilled in the art to which it pertains, or with which it is most nearly connected." In general, the pertinent art should be defined in terms of the problem to be solved rather than in terms of the technology area, industry, trade, etc. for which the invention is used.

The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already

available to the public. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application").< Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976) (In general, if an applicant seeks to use a patent to prove the state of the art for the purpose of the enablement requirement, the patent must have an issue date earlier than the effective filing date of the application.). While a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987).

In general, the examiner should not use post-filing date references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application. In re Hogan,

559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977). If individuals of skill in the art state that a particular invention is not possible years after the filing date, which would be evidence that the disclosed invention was not possible at the time of filing and should be considered. In In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513-14 (Fed. Cir. 1993) an article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms. Claims not directed to the specific virus and the specific animal were held nonenabled. Such is the case with the instant application.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3, 8, 9, 11, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowell et al (Technological Advances in Vaccine Development, 1988, pp 423-432).

Lowell et al discloses isolated meningococcal outer membrane proteins naturally form whole or fragmented hydrophobic membrane vesicles called

proteosomes (abstract). Lowell et al discloses that proteosome vaccines can comprise streptococcal M proteins (abstract; p. 430). The prior art discloses that the proteosomes are safe in people and they are simple to produce (abstract). "The proteosome vaccine system we have developed addresses these problems by using components that are safe for human use and unidirectionally binding peptides to proteins via hydrophobic foot (Hft) that is distant from the epitope. Lowell et al discloses a method of immunizing a subject or individual with the proteosome vaccine system comprising the streptococcal M protein (methods, p. 425).

The prior art anticipates the claimed invention. Since the Patent Office does not have the facilities for examining and comparing applicants' vaccines and methods with the vaccines and methods of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed vaccines and methods and the vaccines and methods of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell et al (Technological Advances in Vaccine Development, 1988, pp 423-432) as applied to claims 1-3, 8, 9, 11, 14 and 16 above, and further in view of Brandt et al (Nature Medicine, 2000, 6/4:455-459).

Lowell et al discloses isolated meningococcal outer membrane proteins naturally form whole or fragmented hydrophobic membrane vesicles called proteosomes (abstract). Lowell et al discloses that proteosome vaccines can comprise streptococcal M proteins (abstract; p. 430). The prior art discloses that

the proteosomes are safe in people and they are simple to produce (abstract). "The proteosome vaccine system we have developed addresses these problems by using components that are safe for human use and unidirectionally binding peptides to proteins via hydrophobic foot (Hft) that is distant from the epitope. Lowell et al discloses a method of immunizing a subject or individual with the proteosome vaccine system comprising the streptococcal M protein (methods, p. 425). Lowell et al discloses the claimed invention except for the claimed amino acid sequence of M protein.

However, Brandt et al teaches preparing a GAS vaccine comprising the portions of the M protein of GAS (abstract). Brandt et al teaches a region of the M protein in identical in 70% of GAS, and that the optimal candidate might consist of the conserved determinant with common N-terminal sequences found in communities with endemic GAS (abstract; Table 1; p. 458, col. 2). Brandt et al teaches the J14 protein which has the amino acid sequence as set forth in SEQ ID NO: 1 and 2 (see methods, p. 458, col. 2). Brandt et al teaches the use of "...highly effective N-terminal epitopes derived from GAS isolates common to a highly endemic region. Because a vaccine with only N-terminal epitopes would still be unable to target all GAS endemic to this region, we included a conserved region epitope, J14, to form the basis of a broad-spectrum vaccine. Such a vaccine might be widely effective, but within a high endemic area would be designed to deliver increased protection by targeting both serotypic and conserved determinants on the M protein." (pp. 457-458) Brandt et al teaches the use of carriers or adjuvants in the vaccine composition such tetanus toxoid, diphtheria toxoid, CFA, or alum (p. 456, col. 1; p. 458, col. 2). Brandt et al teaches that compositions comprising J14 and CFA protected 16 of 19 mice against GAS

challenge and mice immunized with the composition, comprising J14 and PBS, protected 3 of 15 mice (p. 456, col. 1). Further, 8 of 10 mice vaccinated with the J8 peptide linked to diphtheria toxoid and administered with alum survived GAS challenge (p. 456, col. 1).

Lowell et al teaches that small peptides, "...representing protective epitopes of infectious organisms offer great vaccine potential. Peptide vaccine development, however, has been impeded by the insufficient immunogenicity of peptides given without protein carriers and adjuvants. There is currently a paucity of carriers and adjuvants that are safe for human use. Furthermore, it is frequently difficult to covalently conjugate peptides to protein carriers without obscuring or altering the epitope. Moreover, peptide conjugation to routinely used carriers like tetanus toxoid can result in epitope suppression of peptide immunity. The proteosome vaccine system we have developed addresses these problems by using components that are safe for human use and by unidirectionally binding peptides to proteins via a hydrophobic foot (HFt) that is distant from the epitope." (p. 424)

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Lowell et al and Brandt et al since both Lowell et al and Brandt et al teach preparing a vaccine to treat GAS for human use and Lowell et al teaches the need for adjuvants, other than alum, for human use. Brandt et al teaches the use of adjuvants or carriers such as tetanus toxoid or diphtheria toxoid. However, in view of the teachings of Lowell et al that peptide conjugation to routinely used carriers like tetanus toxoid can result in epitope suppression of peptide immunity and that a new adjuvant for human use is needed, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the known M protein of GAS as antigen of

Brandt et al and the proteosome of Lowell et al in a vaccine composition for human use. The claimed invention is prima facie obvious in view of the combined teachings of the prior art, absent any convincing evidence to the contrary.

13. Claims 10-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell et al (Technological Advances in Vaccine Development, 1988, pp 423-432) and Brandt et al (Nature Medicine, 2000, 6/4:455-459) as applied to claims 1-6, 8, 9, 11, 14 and 16 above, and further in view of Relf et al (Advances in Exptal. Med. And Biol., 1997, 418(Streptococci and the Host):859-861.

Lowell et al discloses isolated meningococcal outer membrane proteins naturally form whole or fragmented hydrophobic membrane vesicles called proteosomes (abstract). Lowell et al discloses that proteosome vaccines can comprise streptococcal M proteins (abstract; p. 430). The prior art discloses that the proteosomes are safe in people and they are simple to produce (abstract). "The proteosome vaccine system we have developed addresses these problems by using components that are safe for human use and unidirectionally binding peptides to proteins via hydrophobic foot (Hft) that is distant from the epitope. Lowell et al discloses a method of immunizing a subject or individual with the proteosome vaccine system comprising the streptococcal M protein (methods, p. 425).

Brandt et al teaches preparing a GAS vaccine comprising the portions of the M protein of GAS (abstract). Brandt et al teaches a region of the M protein in identical in 70% of GAS, and that the optimal candidate might consist of the conserved determinant with common N-terminal sequences found in communities with endemic GAS (abstract; Table 1; p. 458, col. 2). Brandt et al teaches the J14

protein which has the amino acid sequence as set forth in SEQ ID NO: 1 and 2 (see methods, p. 458, col. 2). Brandt et al teaches the use of "...highly effective N-terminal epitopes derived from GAS isolates common to a highly endemic region. Because a vaccine with only N-terminal epitopes would still be unable to target all GAS endemic to this region, we included a conserved region epitope, J14, to form the basis of a broad-spectrum vaccine. Such a vaccine might be widely effective, but within a high endemic area would be designed to deliver increased protection by targeting both serotypic and conserved determinants on the M protein." (pp. 457-458) Brandt et al teaches the use of carriers or adjuvants in the vaccine composition such tetanus toxoid, diphtheria toxoid, CFA, or alum (p. 456, col. 1; p. 458, col. 2). Brandt et al teaches that compositions comprising J14 and CFA protected 16 of 19 mice against GAS challenge and mice immunized with the composition, comprising J14 and PBS, protected 3 of 15 mice (p. 456, col. 1). Further, 8 of 10 mice vaccinated with the J8 peptide linked to diphtheria toxoid and administered with alum survived GAS challenge (p. 456, col. 1).

Lowell et al teaches that small peptides, "...representing protective epitopes of infectious organisms offer great vaccine potential. Peptide vaccine development, however, has been impeded by the insufficient immunogenicity of peptides given without protein carriers and adjuvants. There is currently a paucity of carriers and adjuvants that are safe for human use. Furthermore, it is frequently difficult to covalently conjugate peptides to protein carriers without obscuring or altering the epitope. Moreover, peptide conjugation to routinely used carriers like tetanus toxoid can result in epitope suppression of peptide immunity. The proteosome vaccine system we have developed addresses these problems by using components that are safe for human use and by unidirectionally binding peptides to

proteins via a hydrophobic foot (HFt) that is distant from the epitope." (p. 424) Lowell et al and Brandt et al teach the claimed invention except for intranasal administration and prevention or reduction of bacterial colonization of the throat.

However, Relf et al teaches intranasal immunization of mice and the vaccine administered was a GAS based vaccine (title; introduction, p. 859). Relf et al teaches that "...type-specific immunity to GAS infection is long lasting and Abs to the conserved region of M protein increase with age and immune status." (p. 859) "Mucosal immunization has the advantage of inducing immune responses effective at preventing attachment/colonization in the throat (a site of natural infection), and then triggering systemic immunity important for eliminating any invading bacteria." (p. 859) Relf et al teaches the use of various adjuvants (materials and methods, p. 860). Relf et al teaches the production of a serum IgG response as well as IgA and serum IgA (p. 860), which would be indicative of a serum immune response and a mucosal immune response.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Lowell et al, Brandt et al and Relf et al, since all three references teach preparing a vaccine to treat GAS for human use and Lowell et al teaches the need for adjuvants, other than alum, for human use. Brandt et al and Relf et al teach the use of adjuvants or carriers such as tetanus toxoid or diphtheria toxoid. However, in view of the teachings of Lowell et al that peptide conjugation to routinely used carriers like tetanus toxoid can result in epitope suppression of peptide immunity and that a new adjuvant for human use is needed, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the known M protein of GAS as antigen of Brandt et al and Relf et al and the proteosome of Lowell et al in a

vaccine composition for human use. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer the GAS vaccine intranasally since Relf et al teach intranasal immunization with conserved peptides (GAS M protein) linked to cholera toxin subunit B resulted in a significant reduction in pharyngeal colonization of mice following homologous and heterologous GAS challenge. Relf et also teaches that "Mucosal immunization has the advantage of inducing immune responses effective at preventing attachment/colonization in the throat (a site of natural infection), and then triggering systemic immunity important for eliminating any invading bacteria." (p. 859) It would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer the GAS vaccine to an individual, human, since humans are mainly affected by GAS infection. The claimed invention is prima facie obvious in view of the combined teachings of the prior art, absent any convincing evidence to the contrary.

14. No claims are allowed.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
September 8, 2005